REMARKS

The specification has been amended to update the status of the nonprovisional parent application.

Claims 1-44 and 64-70 were pending in the application. In the Office Action dated June 4, 2003, claims 2-7, and 13-18 are withdrawn from consideration as belonging to a non-elected species, claims 23-44 are withdrawn from consideration as belonging to a non-elected group, claims 1, 8-12, 19-21 and 64-70 are rejected, and claim 22 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. In the instant Amendment, claims 23-44 have been canceled, without prejudice, as drawn to a non-elected invention. Applicants reserve the right to pursue the subject matter of the canceled claims in related applications. Claims 1-22, 64 and 70 have been amended to clarify the invention, and new claims 71-72 have been added. Upon entry of the above-made amendment, claims 1-22 and 64-72 will be pending.

Claims 1 and 12 have been amended to clarify that said D_{target} and $D_{off\text{-}target}$ are *each* based on measurements of a plurality of cellular constituents (emphasis added). Support for the amendment is found in the specification at page 35, line 33, through page 36, line 15.

Claim 1 has also been amended to recite that the claimed method comprises comparing activity of said drug against its target pathway and activity of said drug against at least one of its off-target pathways, *thereby evaluating specificity of said drug* (emphasis added). Support for the amendment is found in the specification at page 6, lines 23-25. Claim 1 has also been amended to make the claim language clearer.

Claims 8 and 19 have been amended to clarify that the drug response profile and the perturbation profile each consists of measurements of the same plurality of cellular constituents. Support for the amendment is found in the specification in Equation 5, page 26, lines 1-6. Claims 8 and 19 have also been amended to recite that step c) is for *determining* said D_{target} and $D_{off\text{-}target}$ by comparing said drug response profile and said perturbation profile (emphasis added). Support for the amendment is found in the specification at page 6, lines 23-25.

Claims 9-10 and 20-21 have been amended to correct grammatical errors.

Claims 64 and 70 have been amended to clarify that the drug response profile and the perturbation profile each comprise the same plurality of cellular constituent measurements. Support for the amendment is found in the specification in Equation 5, page 26, lines 1-6.

Claim 64 has been amended to delete from the last thereby clause the phrase "comparing activity of said drug on its target pathway (D_{target}) and at least one off-target pathway ($D_{off\text{-}target}$)."

Claim 70 has been amended such that the claimed method comprises a step of comparing among said one or a combination of pathway response profiles, the pathway response profiles for the one or more biological pathways associated with therapeutic effects of the drug with the pathway response profiles for the one or more biological pathways that are associated with one or more non-therapeutic effects of the drug. Support for the amendment is found in the specification at page 35, line 15, through page 36, line 3; and page 38, lines 11-13.

Withdrawn claims 2-7 and 13-18 have been amended to make the claim language clearer.

New claims 71 and 72 have been added. Support for the new claims is found in the specification at, e.g., page 35, line 33, through page 36, line 16; page 23, lines 18-23 and lines 31-35; and page 38, lines 1-11.

No new matter has been added by these amendments. Entry of the foregoing amendments and consideration of the following remarks are respectfully requested.

THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, SHOULD BE WITHDRAWN

Claims 1, 8-11 and 64-69 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner contends that it is unclear whether the metes and bounds of the claims are defined by the actual active claim steps or by the preamble because the preamble indicates drug specificity evaluation whereas the claim steps are directed to comparing drug activity against target and off-target pathways. Applicants have amended the claims to make it clear that the metes and bounds of the

rejected claims are defined by the actual active method steps, which result in the evaluation of specificity. The rejection is therefore obviated and should be withdrawn.

THE REJECTION UNDER 35 U.S.C. § 103 (a)
SHOULD BE WITHDRAWN

Claims 1, 8-10, 12, 19-21, 64, 69 and 70 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Rine et al., U.S. Patent No. 5,777,888 ("Rine"). The Examiner contends that Rine teaches measurement of a plurality of cellular constituents in response to drugs and analysis of desired effect and side effect to evaluate drug specificity. The Examiner contends that such an evaluation of drug specificity in Rine is deemed to suggest the target vs. off-target pathway evaluation in the instantly claimed invention. The Examiner also contends that the claimed analysis of drug levels and corresponding response profiles is suggested in the Examples in Rine. Applicants respectfully disagree with the Examiner for reasons set forth below.

A finding of obviousness under 35 U.S.C. § 103(a) requires a determination that the differences between the claimed subject matter and the prior art are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere*, 383, U.S. 1 (1956). The relevant inquiry is whether the prior art suggests the invention and whether the prior art provides one of ordinary skill in the art with a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be found in the prior art. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

Rine teaches systems and methods for generating and analyzing stimulated physical matrices, e.g., genome reporter matrices. The stimulated physical matrix of Rine comprises an array of units, each comprising a different responder, e.g., a gene, of a living thing or a probe corresponding to such a responder and an identifier for the responder or probe. The living thing is provided a stimulus, e.g., a drug, capable of repressing the responders of a plurality of the units and the identifiers provide physical signals corresponding to the repression of the respective responders. Rine teaches analyzing such physical matrices by comparing a stimulated physical matrix with a stimulated physical matrix database. Rine also teaches comparing the number of reporters affected by a first drug to the number of

reporters affected by a second drug to determine relative specificity of the first drug to that of the second drug.

With respect to independent claims 1 and 12, Applicants respectfully submit that, although Rine teaches measurement of a plurality of cellular constituents, e.g., as represented by a plurality of units of its physical matrix, Rine does not teach or suggest comparing activity of a drug against its target pathway to activity against its off-target pathway. This is clear because Rine does not distinguish between determining on-target and off-target activities, much less comparing the on- and off-target activities. The Examiner cites column 7, lines 1-16, of Rine. Applicants respectfully points out that the section of Rine cited by the Examiner merely teaches that relative specificities of different drugs that induce the ERG10 reporter can be determined by determining for each drug how many reporters other than ERG10 have expression levels that are altered by the drug, and that the drug that affects a greater number of such other reporters has lower specificity than the drug that affects a lower number of such other reporters. Thus, Rine teaches comparing the number of reporters affected by a first drug to the number of reporters affected by a second drug to determine relative specificity of the first drug to that of the second drug. In Rine, there is no teaching of comparison of on-target vs. off-target activity of a particular drug. For example, determining the number of reporters as taught by Rine does not provide a value for on-target activity. Thus, Rine does not teach comparing on-target vs. off-target activities for a drug in order to evaluate the specificity of the drug. Even assuming, arguendo, that the "other reporters" measured in Rine in order to evaluate specificity of two drugs represent off-target activities (since they are reporters other than ERG10), this is merely a comparison of off-target activities of two different drugs, rather than a comparison of on-target to off-target activities of one drug. The specificity of Rine is relative specificity of one drug to another drug, requiring comparison of data of one drug to data of a second drug, not comparison of data for one drug alone. There is no teaching or suggestion in Rine of determining activity of a drug against its target pathway based on a plurality of cellular constituents. As such, Applicants respectfully submit that the invention as claimed in claims 1 and 12, and the claims dependent thereon, are nonobvious under 35 U.S.C. § 103 (a) over Rine, and that the rejection of these claims under 35 U.S.C. § 103 (a) over Rine should be withdrawn.

With respect to independent claims 64 and 70, Applicants respectfully submit that Rine does not teach or suggest decomposing a drug response profile into one or a

combination of pathway response profiles, wherein the drug response profile comprises measurements of a plurality of cellular constituents in a biological sample in response to the drug over a plurality of levels of drug exposure, and each pathway response profile comprises measurements of the plurality of cellular constituents at a plurality of levels of perturbation to a biological pathway. Applicants respectfully direct the attention of the Examiner to Section 5.1.4. for a description of the method of decomposing drug responses into pathway responses. Nor does Rine teach or suggest evaluating specificity of the drug by comparing, among the one or a combination of pathway response profiles, the pathway response profiles for the one or more biological pathways associated with therapeutic effects of the drug with the pathway response profiles for the one or more biological pathways that are associated with one or more non-therapeutic effects of the drug. A person of ordinary skill in the art would not be motivated with a reasonable expectation of success to decompose a drug response profile comprising measurements of a plurality of cellular constituents in a biological sample in response to the drug over a plurality of levels of drug exposure into one or a combination of pathway response profiles, each of which comprising measurements of the plurality of cellular constituents at a plurality of levels of perturbation to a biological pathway, much less evaluating specificity of the drug by comparing, among the one or a combination of pathway response profiles, the pathway response profiles for the one or more biological pathways associated with therapeutic effects of the drug with the pathway response profiles for the one or more biological pathways that are associated with one or more non-therapeutic effects of the drug. Thus, Applicants respectfully submit that the invention as claimed in claims 64 and 70, and the claims dependent thereon, are nonobvious under 35 U.S.C. § 103 (a) over Rine, and that the rejection of these claims under 35 U.S.C. § 103 (a) over Rine should be withdrawn.

THE OBJECTION TO CLAIM 22 SHOULD BE WITHDRAWN

Claim 22 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. As discussed above, the base claim 12, upon which claim 22 depends, is not rendered obvious by Rine. Therefore, the objection to claim 22 should be withdrawn.

CLAIMS WITHDRAWN FROM CONSIDERATION AS BELONGING TO NON-ELECTED SPECIES SHOULD BE CONSIDERED

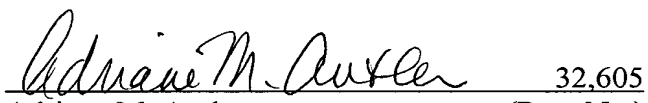
Claims 2-7 and 13-21 were withdrawn from consideration by the Examiner as belonging to non-elected species. Since Applicants believe that the generic claims are allowable, claims 2-7 and 13-21 should be considered by the Examiner. Applicants respectfully request that these claims be considered by the Examiner.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks into the file of the above-identified application. Applicants believe that all the pending claims are in condition for allowance. Withdrawal of the Examiner's rejections and allowance of the application are respectfully requested.

Respectfully submitted,

Date: October 3, 2003



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